

## REMARKS / ARGUMENTS

Upon entry of the present amendments, claims 7-9 are pending. Claims 7-9 are amended herein. The foregoing amendments are made without any intention to abandon the subject matter of the claims as filed, but with the intention that claims of the same, lesser or greater scope may be pursued in the present application or in a continuation, continuation-in-part or divisional applications. Applicants believe that the present amendment does not add new matter.

Support for the claim amendments can be found in the claims and the specification, as follows:

Claim 7 has been amended to recite: An isolated human neurotrophic polypeptide, said polypeptide comprising the amino acid sequence of SEQ ID NO:3, or a functional equivalent derivative thereof. Support for this amendment can be found *inter alia* in originally-filed claims 7-9 and in the Specification at least at page 4, lines 27-end; page 11, lines 14-end, through page 13, lines 1-2; page 12, line 24 through page 13, line 11; page 25, lines 18-end through page 26, lines 1-2; page 42, line 29 through page 43, line 32; and FIGS. 1, 22-24. Support can be found in all priority applications, for example in USSN 09/327,668 support can be found in at least page 4, lines 27-end; page 20, lines 24-end, through page 21, lines 1-6; page 10, lines 16-end, through page 12, lines 1-9 and FIG. 1. In USSN 09/248,772 support is found in at least page 4, lines 27-end; page 15, lines 9-26; page 9, lines 14-end, through page 10, lines 1-32; and FIG. 1. In UK 9815283.8 support is found in at least page 4, lines 15-23; page 12, lines 14-21; page 8, lines 3-end, through page 9, lines 1-5 and FIG. 1.

Claim 8 has been amended to recite: The isolated neurotrophic polypeptide of claim 7, wherein the derivative has at least 90% homology to SEQ ID NO:3. Support for this amendment can be found *inter alia* in originally-filed claim 41 and in the Specification at least at page 13, lines 3-11; FIGS. 22-24, and SEQ ID NO:9-10. Support can be found in all priority applications, for example in USSN 09/327,668 support can be found in at least page 12, lines 5-9. In USSN 09/248,772 support can be found in at least page 10, lines 23-32. In UK 9815283.8 support can be found in at least page 4, lines 31-end, through page 5 lines 1-13.

Claim 9 has been amended to recite: The isolated neurotrophic polypeptide of claim 8, wherein the derivative is SEQ ID NO:9 or SEQ ID NO:10. Support for this amendment can be

found *inter alia* in the Specification at least at page 42, line 29 through page 43, line 32; FIGS. 22-24, and SEQ ID NO:9-10. The functional equivalent derivatives described in SEQ ID NO:9-10 have greater than 90% homology with SEQ ID NO:3. Support can be found in all priority applications, for example in USSN 09/327,668 support can be found in at least page 11, lines 24-35 through page 12, lines 1-9; page 35, line 34-35 through page 36, line 1-8 and FIG. 22. In USSN 09/248,772 support can be found in at least page 9, lines 18-35; page 10, lines 11-31. In UK 9815283.8 support can be found in at least page 8, lines 3-18; page 8, lines 29-end through page 9, lines 1-5.

Each of the grounds of rejections in the May 17, 2004 Office Action will be addressed in turn below:

### **Election/Restriction**

The Examiner has acknowledged Applicants' election of Group I, claims 7-9 (polypeptide of SEQ ID NO: 3). Applicants have amended claims 7-9 to be drawn to the elected polypeptide of SEQ ID NO: 3, in accordance with the requirement for restriction.

### **Claim Objections**

The Examiner has objected to claim 8 as missing a conjunction. Claim 8, as amended herein, no longer contains the objected-to language. Accordingly, Applicants request reconsideration and withdrawal of the present objection.

The Examiner further objected to claim 8 as substantially duplicative of claim 7. Applicants have amended Claim 8 herein to define the functional equivalent derivatives of SEQ ID NO:3. Accordingly, Applicants request withdrawal of the present objection.

### **35 U.S.C. §112**

Claim 8 stands rejected under 35 U.S.C. §112, second paragraph, as indefinite. Applicants respectfully traverse this rejection in view of the present claim amendments.

Applicant has amended the claims to define the claimed polypeptide in terms of the amino acid in SEQ ID NO:3. Accordingly, Applicants request reconsideration and withdrawal of the present rejection.

### **35 U.S.C. §102**

Claims 7-9 are rejected under 35 U.S.C. § 102(e) as being anticipated by Johansen *et al.*, U.S. Patent No. 6,593,133 (hereinafter, "Johansen *et al.*"). The earliest priority date of Johansen *et al.* is July 9, 1998.

Claims 7-9 are further rejected under 35 U.S.C. § 102(e) as being anticipated by Milbrandt *et al.*, U.S. Patent No. 6,284,540 (hereinafter, "Milbrandt *et al.*"). The earliest priority date of Milbrandt *et al.* is September 29, 1998.

Applicants submit herewith a Declaration of Prior Invention under 37 C.F.R. § 1.131. As detailed in the Declaration, the Applicants were in possession of the invention which is the subject of Applicant's above-identified patent application prior to July 9, 1998. Accordingly, Applicants assert they had possession of the invention prior to the earliest filing dates of the Johansen *et al.* and Milbrandt *et al.* references. In the Declaration, Applicants present two pages from a draft patent application, provided to Applicants attorney prior to July 9, 1998. Applicants hereby preserve the right to establish an earlier date of invention in the future using additional evidence which predates the facsimile referenced in the present Declaration of Prior Invention under 37 C.F.R. § 1.131. Accordingly, the Applicants traverse the rejection of claims 7-9 under 35 U.S.C. § 102(e). For this reason, the rejection of claims 7-9 under 35 U.S.C. § 102(e) is moot for both references. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §102(e) rejection.

### **CONCLUSION**

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Appl. No.: 09/357,349

Amendment and Response dated Nov. 17, 2004

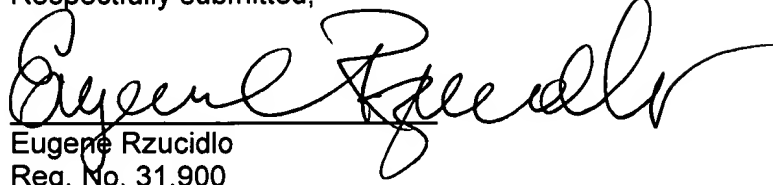
Amendment and Response to May 17, 2004 Office Action

Express Mail No.: EV 316 900 654 US

Date of Deposit: November 17, 2004

Dated: November 17, 2004

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Eugene Rzucidlo", written over a horizontal line.

Eugene Rzucidlo

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P F Q F S R P A P P P P A P P S	16
cgccgcccagccttctcggcccgagcccccggcgctgcacccccatct	50
A L P R G G <b>R A A R</b> A C G P G S R	33
gctcttcccccgagggggccgcccggcggggtggggggcccgggcagccg	100
A R A A G A R G C R L R S Q L V	49
cgcctcgggcagcggggcgcggggctgccgcctggcgctgcagctgggtgc	150
P V R A L G L G H R S D S L V R F	66
cggtgcggcgcgctcggcctggggccacgcgtccgacgagctgggtgcgtttc	200
R F C S G S C R R A R S P H D L S	83
cgccttctgcagcgggtcctgcgcgcgcgcgcgtctccacacgacctcag	250
L A S L L G A G A L R P P P G S	99
cctggccagcctactggggcgccggggccctgcgacgcggcccggggtccc	300
R F V S Q P C C R P T R Y E A V S	116
ggcccgctcagccagccctgctgcgcgacccacgcgctacgaagcggtctcc	350
P M D V <b>N S T</b> W R T V D R L S A T	133
ttcatggacgtcaacagccacctggagaaacgctggacgcctctccgccac	400
A C G C L G *	139
cgcccgggctgcctggggctgaggggtcgctccaggggtttgcagactgg	450
acccttacgggtgggtctcttcctgcg	474

Figure 1; Partial cDNA sequence of enovin. The consensus sequence was obtained by PCR amplification with primers PNHsp3 and PNHsp1 on different cDNAs and on genomic DNA followed by cloning and sequence analysis and comparison of the obtained sequences. The predicted one letter code amino acid sequence is shown above the DNA sequence. The nucleotide residue number is shown to the right of the DNA sequence, whereas the amino acid residue number is shown to the right of the translated protein sequence. The putative RXXR cleavage site for the prodomain is indicated in bold and underlined. The putative start of the mature protein is indicated by an arrow. The seven conserved cysteine residues characteristic for all members of the TGF- $\beta$  family are indicated in bold. A potential N-glycosylation site is double underlined.



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hGDNF : SPDKQMAVLPRRERNRQAAAANFENSRRKRRGGGNN : 40
hNTN : -----AATLSP : 7
hPSP : -----LSCG : 5
hEVN : -----AGPSSKARAA : 15
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hGDNF : VVATHTNITDDEETKELPSSDDEETTY : 79
hNTN : GGEVRSSESTLPAEELARVY : 46
hPSP : QETSTSAEETKYPPEPRG : 45
hEVN : RRSQVLRALERRRRLRRFERRRRSSPH : 54
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hGDNF : KIKRMGRNRVSG---DKVLAITFDL : 115
hNTN : EIGRRRRRR---EVRALRR : 83
hPSP : GLAELQOC---AHEG---RT- : 76
hEVN : RRSSTLAAARPPGSPSSRRRRR-ARSG : 93
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hGDNF : DNLVYHTRKHARRRI- : 134
hNTN : AHEVYEVHEAREAV- : 102
hPSP : RRHRRRPPQAA : 96
hEVN : VETRRVDRRRT : 113
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Figure 2; Alignment of the predicted mature protein sequences of human GDNF, NTN, PSP and EVN. The sequences were aligned using the ClustalW alignment program. Amino acid residues conserved between all three proteins are included in the black areas. Residues conserved between two or three of the sequences are shaded in grey. The 7 conserved cysteine residues characteristic for members of the TOF- $\beta$  family are indicated by asterisks above the sequence. Amino acid residues are numbered to the right. The dashes indicate gaps introduced into the sequence to optimize the alignment.